New Insights Into Selecting Asymptomatic Carotid Stenosis Patients At High Stroke Risk Who Should Have CAS Or CEA: The Importance Of Juxtaluminal Black Areas.

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Prospective natural history studies indicate that with modern medical therapy the overall risk of stroke has been reduced to 1% (1) and there is a strong argument that patients with asymptomatic carotid stenosis should not be operated on. Therefore, there is a need to identify high risk subgroups.

Carotid plaques produce emboli leading to TIAs or stroke because they rupture or have a thrombus on their surface. It has been demonstrated that the prevalence of preoperative silent embolic infarcts on CT-Brain scans is 62% in patients with ulcerated carotid endarterectomy specimens compared with 8% in the absence of such ulceration (2).

Prospective studies in patients with asymptomatic carotid stenosis have demonstrated that three methods are able to identify high risk subgroups for stroke: (a) Transcranial Doppler (TCD), (b) CT-Brain scans and (c) Ultrasonic plaque imaging.

**TCD Embolic Signals:**

In the ACES study, which involved 467 asymptomatic patients (mean follow-up 2 years) with ≥70% internal carotid stenosis, the presence of TCD microembolic signals during a recording for one hour could identify a subgroup with a 7.5% annual stroke rate (3). A meta-analysis of 6 prospective studies including the ACES has confirmed these results (3). TCD microembolic signals are found in 15-20% of patients with asymptomatic carotid stenosis and characterize patients that constitute a high risk group. However, this group contains only 57% of the strokes that occur during follow-up. Thus, 47% of the plaques that will produce a stroke will be missed.

TCD recording for an hour may not be enough to detect all unstable plaques or some plaques may rupture and produce emboli without prior microembolization.

**Silent Infarcts on CT-Brain Scans:**

The prevalence of silent infarcts on CT-Brain scans in patients with asymptomatic carotid stenosis varies from 10-24% (4-6). The presence of embolic infarcts (small cortical, discrete subcortical, basal ganglia non-lacunar infarcts) can identify a high risk group with an average annual stroke risk of 3.6% (7). However, this group contains only 30% of the strokes that occur during follow-up. Thus, 70% of the plaques that will produce a stroke will be missed. Also, this means that plaques rupture producing strokes without giving off prior emboli that result in silent infarcts.

**Ultrasonic Plaque Features:**

Several factors that have been proposed to predict stroke in patients with asymptomatic carotid stenosis and thus contribute to risk stratification, have been confirmed in prospective studies. They include severity of stenosis (8), low gray scale median (GSM) (9,10), plaque area ≥80 mm sq, a history of contralateral TIAs or stroke, the presence of a juxtaluminal black plaque area
without a visible echogenic cap (JBA) ≥8 mm sq (11) and the presence of discrete white areas (DWA) without acoustic shadowing indicating neovascularization (9).

In the ACSRS study which involved 1121 patients with asymptomatic carotid stenosis ≥ 50% and a mean follow-up of 4 years, a GSM < 30 was found in 22% of plaques. It identified a high risk group with an average annual stroke risk of 3.0% (9). However, this group contained only 54% of the strokes that occurred during follow-up. In contrast, the presence of a JBA ≥8 mm sq identified a high risk group with an average annual stroke risk of 4.1% (11). This group contained 71% of the strokes that occurred during follow-up.

Key Message:
A key message that emerges is that there is not a single feature that can identify all the potentially unstable and high risk plaques. This is because there are several mechanisms that result in embolization. Some plaques produce emboli because of a thrombus on their surface, some because they rupture having a large lipid core and a thin fibrous cap, while others rupture because of mechanical forces irrespective of their structure. Thus, a combination of plaque features should perform better than a single feature alone.

Combined Features:
In the ACES study, TCD microembolic signals and plaque echolucency have been shown to be independent predictors of risk and the presence of both could identify a subgroup with a 17% annual stroke rate (12).

In the ACSRS study, four features have now emerged as independent predictors of risk: degree of stenosis, history of contralateral TIAs or stroke, a JBA ≥ 8 mm sq and the presence of DWAs. These 4 features, which are independent of ultrasonic equipment used, can be used to calculate risk for every patient (range: < 1% to 10% per year) (10). In the ACSRS study the risk was < 1% in 734 patients, 1.1-1.9% in 94 patients, 2.3-3.9% in 134 patients, 4.1-5.9% in 125 patients and 6-10% in 34 patients.

Capturing the appropriate views of plaque images using ultrasound should be within the capability of every vascular ultrasonographer. Image normalization and measurement of JBA size using commercially available software is relatively simple on a laptop adding an extra 10 minutes to the examination. Risk stratification is now provided by a limited number of vascular laboratories, when requested. With increasing awareness and demand, risk stratification should become more widespread.

Conclusions:
1. The above studies should be repeated in patients having modern medical therapy which is expected to reduce stroke by 50%.
2. In the meantime, even if we calculate the risk of a patient using any of the above methods and divide it by 2 to allow for the effect of modern medical therapy, there will still be many patients with an annual stroke risk greater than 2%.
3. In 2013, it is no longer appropriate to operate on patients with asymptomatic carotid stenosis without the use of any of the available methods described above to stratify
patients into different risk categories. Already, several vascular surgeons and neurologists expect risk stratification to be part of a patient’s vascular work-up.

References:

1. Abbott AL. Medical (nonsurgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. Stroke 2009;40:e573-83


